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REMARKS

Claims 24-28 are pending in the Subject Application. Claim 24 has been amended.

Support for amended claim 24 can be found in the Specification as originally filed, see for example, Example 8, which describes implantation of transformed cells, in the absence of mounting the cells on collagen sponges, for example as described in Example 11. No new matter has been introduced.

THE TELEPHONE INTERVIEW

Applicants wish to thank Examiner Popa for the telephone interview of November 5, 2007. In the telephone interview, Examiner Popa indicated that claims to the use of human BMP-2 transduced MSC administered in the absence of an exogenously supplied matrix to recipients to promote organized bone formation would be novel and unobvious, and supported by the Examples in the Specification.

REJECTION UNDER 35 U.S.C. § 103:

In the Office Action, the Examiner rejected claims 24-28 under 35 U.S.C. § 103 as allegedly being rendered obvious in view of Bruder et al. (J Cell Biochem., 1994, 56: 283-294) and Bonadio, previously cited.

The Examiner alleged that Bruder describes use of MSC in combination with BMP-2 in bone repair, and describes the importance of autocrine and paracrine effects of such cells. The Examiner admits that Bruder does not disclose transforming MSC with a BMP-2 expressing construct. The Examiner alleges that Bonadio describes using MSC transformed to express BMP-2 to treat bone defects.

The Examiner alleged that there is motivation to combine the two as the art recognizes the short half-life of BMP-2 and PTH, and transformation yields longer protein expression at the site, and the art teaches that the compositions can be successfully made and used.

Applicants disagree. Applicants maintain that Bruder specifically describes that MSC must be administered in an appropriate matrix [Page 291, Column 1, second paragraph]:

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"In order to effect osseous repair in a local defect, *the cells must be delivered to the site in an appropriate carrier* (*emphasis added*). We envision the ideal vehicle as biocompatible to minimize inflammation, osteoconductive to foster integration, resorbable to promote its own replacement, supportive of mesenchymal stem cell attachment and porous to facilitate rapid vascularization. In many ways, this vehicle would functionally resemble hypertrophic cartilage of the growth plate or fracture callus".

Applicants submit that Bruder (citing Wozney) refers to an absolute requirement for an osteoinductive matrix, a point raised by the Applicants in several recent responses to Office Actions, including the most recent response of February 20, 2007.

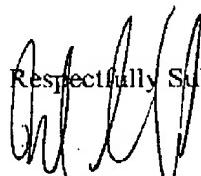
Since Bruder acknowledges an absolute requirement for a matrix, and since Bonadio is not a credible reference for describing transformation of MSCs, as noted in the Declaration supplied on Feb. 20th, 2007, thus one skilled in the art, would necessarily expect that MSC alone engineered to express BMP-2 would not be sufficient to stimulate bone formation.

Moreover, Applicants have herein demonstrated that unexpectedly, only MSC expressing BMP-2 (MSC-BMP-2) provided superior bone formation, which aligned along the bone defect edge. Surprisingly, only MSC-BMP-2 yielded such superior effects, this despite the fact BMP-2 was secreted at a roughly 100 times lower concentration than that of CHO cells transduced to express BMP-2 and 100 times lower concentration than the amount of BMP-2 loaded on collagen sponges. Despite significant reduction in BMP-2 secretion, nonetheless, only MSC-BMP-2 appropriately homed to the site of injury, aligned along defect edges, was incorporated in newly formed bone trabecules, and formed superior quantitative and qualitative bone, with less bone resorption, as compared to non-transduced MSC, or CHO-BMP-2, or sites of implantation of collagen sponges comprising the BMP-2 alone.

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Based on the foregoing, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested. Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below.

Should any fee be due, the undersigned Attorney hereby authorizes the United States Patent and Trademark Office to charge Deposit Account No. 50-3355 for any fees required.


Respectfully Submitted,

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